

# RECENT EXPERIMENTAL RESEARCH BEARING UPON BLACKWATER FEVER

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In 1909 Barratt and Yorke\* in an investigation into the mechanism of production of blackwater showed that in this condition haemoglobinuria was preceded by, and dependent upon, haemoglobinaemia. It was also shown that suppression of urine, occurring in blackwater fever, was due to mechanical blocking of the uriniferous tubules. In one experiment in which haemoglobinaemia was induced in a rabbit by the injection of haemoglobin, death occurred suddenly at the end of eighty-five minutes; in all similar experiments, however, the general condition of the animals injected was not affected.

As subsequent papers bearing upon these observations are somewhat scattered it will be of advantage to give a brief résumé of the results obtained.

Barratt† (1910), in order to ascertain the extent to which the haemolytic action of quinine salts upon red blood cells was due to hydrolytic dissociation, determined the first and second dissociation constants of this alkaloid.

Barratt and Yorke‡ (1909) extended their observations to piroplasmiasis in the dog, and showed that in this condition haemoglobinuria makes its appearance as soon as the blood plasma contains as much haemoglobin as is obtainable from an amount of red cells equal to 0.5 per cent., by volume, of the plasma, the

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\* J. O. W. BARRATT and W. YORKE. 'An investigation into the Mechanism of Production of Blackwater.' *Annals of Trop. Med. & Parasit.*, 1909, Vol. III, p. 1.

† J. O. W. BARRATT. 'Über die Konstanten der ersten und zweiten Dissociation des Chinins.' *Zeitschr. f. Elektrochemie*, 1910, B. 16, S. 130.

‡ J. O. WAKELIN BARRATT and W. YORKE. 'Über den Mechanismus der Entstehung der Hämoglobinurie bei Infektionen mit *Piroplasma canis*.' *Zeitschr. f. Immunitätsforschung u. exp. Therapie*, 1909, B. 4, S. 313.

percentage of haemoglobin in the urine being generally considerably greater than that contained in the blood plasma. Haemoglobinaemia and haemoglobinuria do not make their appearance in this condition until an extensive destruction of red cells has taken place, the latter often showing at the time of death a diminution to one-fifth of the number originally present; the plasma, on the other hand, remains little altered in volume. In two cases jaundice was observed.

Yorke and Nauss\* (1911) showed that the injection of a haemoglobin holding fluid in sufficient amount was frequently followed by severe symptoms, rapidly terminating in death. In this connection attention may be directed to the severe symptoms attending blackwater fever during the period of haemoglobinuria; the similarity of the symptoms in the two cases suggests that the mechanism of production is the same in both. Yorke and Nauss also made the important observation that suppression of urine in some cases followed the injection of a solution of haemoglobin. It was found that this result was obtained if a sufficient amount of the haemoglobin was injected in an animal which had previously been deprived of water for some time, the occurrence of a greatly increased secretion of urine, which would otherwise follow upon injection, being thus prevented.

Yorke† (1911) observed that, in haemoglobinaemia due to *Piroplasma canis* or produced by the intravenous injection of haemoglobin, granules reaching as much as  $3\mu$  in diameter were found in large numbers in the epithelium of the convoluted tubules of the kidney, indicating that the seat of elimination of haemoglobin is the epithelium of these tubules. Illustrations are given of sections of the kidney after injection.

Barratt and Yorke‡ (1912) in the course of a further investigation showed that the acute symptoms following injection were not attributable to haemoglobin, but to substances derived from the stromata of the red cells. For the production of anuria the

\* W. YORKE and R. W. NAUSS. 'The Mechanism of the Production of Suppression of Urine in Blackwater Fever.' *Annals of Trop. Med. & Parasit.*, 1911, Vol. V, p. 287.

† W. YORKE. 'The passage of Hamoglobin through the Kidneys.' *Annals of Trop. Med. and Parasit.*, 1911, Vol. V, p. 401.

‡ J. O. W. BARRATT and W. YORKE. 'Ueber Hämoglobinämie.' *Zeitschr. f. Immunitätsforschung u. exp. Therapie*, 1912, B. 12, S. 333.

introduction of haemoglobin in relatively large amounts into the circulating blood was shown to be necessary, but here also the presence of substances derived from the stromata was found to be a factor in the determination of anuria. The blood generally coagulated less rapidly after the injection of a solution of haemoglobin. The observations made did not, however, admit of a conclusion being arrived at as to the exact mode in which the general symptoms following injection were brought about. In a subsequent investigation\* by the same observers these conclusions were confirmed.

Barratt† (1913) pointed out that the granules in the convoluted tubules of the kidney, observed in the course of haemoglobinaemia, represent mitochondria, which in this condition become remarkably enlarged, and are very readily stained.‡

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\* J. O. W. BARRATT and W. YORKE. 'The Production of general symptoms in haemoglobin-aemia.'

† J. O. W. BARRATT. 'Changes in Chondriosomes occurring in pathological conditions.' *Quart. Journ. of Micro. Sci.*, 1913, Vol. LVIII, p. 553.

‡ In this connection it may be pointed out that Lebedeff ('Zur Kenntniss der feineren Veränderungen der Nieren bei Hämoglobinausscheidung.' *Virch. Arch.*, 1883, B. 91, S. 267) and Afanassiew ('Über die pathologisch-anatomisch Veränderungen in den Nieren und in der Leber bei einigen mit Hämoglobinurie oder Icterus verbundenen Vergiftungen.' *Virch. Arch.*, 1884, B. 98, S. 460) both give illustrations of the condition of the kidney in haemoglobinuria, in which the chondriosomes of the convoluted tubules appear to be imperfectly represented. Marchand ('Über die Intoxication durch chloresaurer Salze.' *Virch. Arch.*, 1879, B. 77, S. 455) regarded the elimination of red blood cells and portions of red blood cells as taking place through a kind of diapedesis; the structures in question being evidently hypertrophied mitochondria, which form striking objects in sections of the kidney during marked haemoglobinaemia.